UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,744	01/30/2004	Anna Helgadottir	30847/2051-004	6429

4743 7590 03/13/2008
MARSHALL, GERSTEIN & BORUN LLP
233 S. WACKER DRIVE, SUITE 6300
SEARS TOWER
CHICAGO, IL 60606

EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
03/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,744	HELGADOTTIR ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *206-228* is/are pending in the application.

4a) Of the above claim(s) *210,215 and 218-224* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *206-209,211-214,216,217 and 225-228* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed **11/30/07** presents remarks and arguments to the office action mailed **6/01/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Claims 207 and 214 has been added to the claims. Argument persuasive.

Status of Claims

Claims 206-228 are pending. Claims 210, 215, 218-224 are withdrawn and claims 206-209, 211-214, 216-217 and 225-228 are examined in this office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/30/07 have been received and acknowledged.

Items C121-C129 remains unconsidered because they are not considered published documents. Individual prior art identified in the search note should be listed and not refer to the search record as non-patent literature.

Maintained Claim Rejections - 35 USC § 112

Applicant argues that the prodrug recited in claim 212 would be metabolized into BAY-1005.

In response, Applicant is claiming a prodrug that has not been disclosed. Claim 212 recites BAY-X-1005 or a prodrug thereof without stating what the prodrug is. The rejection is therefore maintained.

Claims 212 and 213 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. In the specification the mention of prodrugs is acknowledged in paragraphs 0336, 0339 and 0349 but fail to show what these prodrugs are. In particular, Applicant has not provided a description of the structure of a representative number of derivative compounds nor a description of the chemical and/or physical

characteristics of a representative number of compounds nor a description of how to obtain a representative number of specific compounds.

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims **206-209, 211-214 and 216-217, 226 are** rejected under 35 U.S.C. 103(a) as being unpatentable over Hatzelmann et al. Agents Actions 43: 64-68 (1994) taken with Mazzone et al. J. Am. Coll. Cardiology, 2001;38: 1895-1901 and Pietila et al. European Heart J. 1996 17,1345-1349 in view of Rossoni et al. The J. of Pharm. and Exp. Ther. Vol. 276;335-341 1996 taken with Muller-Peddinghaus et al. and Gompertz et al. Chest vol.122, 289—294, 2002 and Cunningham et al. Journal of Veterinary Pharmacology and Therapeutics 20 (4) , 296– 307 Abstract Only.

Hatzelmann et al. teach administering BAY-X-1005, the claimed compound for the inhibition of inflammatory disease. It is the understanding that the compound is a FLAP inhibitor as required. See underlining page 64-abstract. The reference is silent of the teaching of myocardial ischemic as required by 2006. The drug is orally administered, see underlining rt. col. of introduction. Teaching of claims 206, 211-213. As to an effective amount, the claim is obvious since it teaches the inhibition of FLAP it would have been obvious that an effective amount was administered as required by instant claim 214. Although it is not clearly stated that the leukotriene levels is monitored, the reference however suggest that the compound is a binding leukotrien synthase inhibitor as underlined in the abstract and introduction.

Mazonne et al. teach as evidence that myocardial ischemic correlates to inflamation.

Pietila et al. teach C-reactive protein is evident of acute myocardial infaction see underlining page 1345. C-reactive protein is an acute phase reactant , its serum concentration rises due to various inflammatory stimuli, including myocardial infaction. See underling page 1346 as required by instant claim 206, 207 and 226.

One of ordinary skill in the art would have combined the cited reference of hatzelmann, Mazonne and Pietila to arrive at the claimed invention because BAY-X-1005 has been used to treat inflammatory disease. It is taught the myocardial ischemic is an inflammatory disease. It would have been obvious to one of ordinary skill in the art to use the claimed compound for myocardial ischemic because it known in the art to treat inflammatory disease and as clearly seen by Mazone myocardial ischemia correlates to high cytokine production an inflammatory indicator. Also that myocardial ischemic is the cause of high concentrations of c-reactive protein. The drug is orally administered, see underlining rt. col. of introduction.

Rossoni et al. teach, monitoring leukotriene administering BAY-x-1005 (see abstract) wherein 20% reduction was seen with a significant protection against the increase in coronary perfusion pressure (see abstract). The Rossoni reference also teaches the BAY-X-1005 exerts a significant cardioprotection.

Muller-Peddinghaus et al. teach BAY-X-1005 as an orally active inhibitor of leukotrienes (see abstract first two lines).

Gompertz et al. teach the administration (orally) of Bay-X-1005 (see abstract) monitoring the leukotriene in the patients, wherein the monitoring is from spontaneous sputum samples monitoring LTB_4 showed that leukotriene synthesis inhibitor BAY-X-

1005 reduces LTB_4 in human subjects as in claims 216 and 217 (see page 290, rt. col.). As to claim 217, the reference teaches blood (see page 293 rt. col. underlined) and the knowledge of one of ordinary skill in the art know knows that blood is approximately 55% plasma, thus teaches the claimed invention. As to claim 207, the MI agent inhibits leukotriene synthesis by inhibiting the activity of lipoxygenase activating protein (FLAP) (see page 292, highlighted sec.)

Cunnigham et al. teach The 5-lipoxygenase activating protein (FLAP) inhibitors, BAY X 1005 and BAY Y 1015, produced concentration dependent inhibition of ionophore-induced LTB4 of whole blood. See underling abstract..

One of ordinary skill in the art would have been motivated to combine the above cited art, monitor the patient serum (plasma) level by first assaying for patients with high levels of leukotriene proteins, since the reference used BAY-X-1005 to inhibit leukotrien levels.

One of ordinary skill in the art would have been motivated to use the above teaching monitor the leucotriene level in a patient before and after the administering step because since the drug is a inhibitor of leukotriene activity, wherein the drug has shown to inhibit (lower) the 5-LOX activating protein. It is well within the knowledge of one of ordinary skill in the art to know how the inhibition is carried out by first determining the leukotriene level before administering the drug BAY-X-1005 and after administration. These are common practice within the level of one of ordinary skill in the art (see Gometz page 292-graphs) wherein the baseline was determined and after 14 days.

Thus, the instantly claimed method using the claimed compound BAY-X-1005 would have been successful when used in the treatment of myocardial infarction as shown in the references cited.

Claims **225, 227-228 are** rejected under 35 U.S.C. 103(a) as being unpatentable over Hatzelmann et al. Agents Actions 43: 64-68 (1994) taken with Mazzone et al. J. Am. Coll. Cardiology, 2001;38: 1895-1901 and Pietila et al. European Heart J. 1996 17,1345-1349 in view of Rossoni et al. The J. of Pharm. and Exp. Ther. Vol. 276;335-341 1996 taken with Muller-Peddinghaus et al. and Gompertz et al. Chest vol.122, 289—294, 2002 and Cunningham et al. Journal of Veterinary Pharmacology and Therapeutics 20 (4) , 296– 307 Abstract Only as applied to claims **206-209, 211-213 and 216-217, 226** above further in view of Byrum et al. J. Exp. Med Vol. 185(6) 1065-1075 1997.

Hatzelmann et al teach BAY-X-1005 is a five lipogenase activating protein. One of ordinary skill in the art knows that genes code for proteins absent factual evidence.

Byrum et al. reference did not teach explicitly the determination of Flap genotype in humans, however, the reference teaches identification of the FLAP genes in animal (mice) and showed that when the genotype is missing, reduced inflammatory response is seen (see page 1073). Even though humans are not used in the genotypying, but the knowledge that cardiovascular complication that accompanies an inflammatory response induced by leucocytes in myocardial tissue, one of ordinary skill in the art would be motivated to use BAY-X-1005 and administer to the subset of patients with a Flap genotype, and lack of FLAP and leukotrienes will result in a detectable attenuation

in hypersensitive patients. Therefore one of ordinary skill in the art would be motivated to transfer from the use of animals to humans and administer BAY-x-1005 to patients with a FLAP genotype.

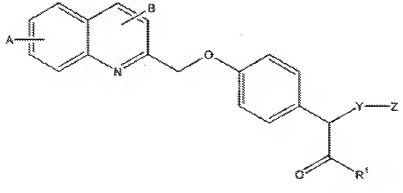
Maintained Double Patenting

Applicant's request that the Double Patenting rejection be held in abeyance until it is made permanent is noted but will be maintained in this Office Action and future Office Actions until withdrawn. Applicants, have not presented a terminal disclaimer and the claims of the above co-pending rejection remain pending , since this is not the only or sole rejection remaining the rejection is properly maintained.

Claims 206-209, 211-214, 216-217 and 225-228 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1-7, 25-31 and 32-41** of U.S. Patent Application No. **11270804**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

The claims of the instant application with that of the co-pending application refer to a method of treating/prophylaxis therapy for myocardial infarction in human comprising administering a MI agent that inhibits leukotriene synthesis in vivo.

Both applications recite using the compounds such as BAY-x-1005



. See current

application claims 206-209, 211-214, 216-217 and 225-228 and copending application claims 1, 27-30, 32-36 and 38-41.

As to the copending application claims 1-7, these claims refer to a process of identifying a nucleic acid with a genotype that correlates with race with MI in atleast one gene, therefore the instant application would have resulted in the intermediate process in screening, and since these genotypes are specific for MI the screening would have been used in the claimed process of claims 206-210, 212-222 and 245-246 in the instant application because they would have been used in producing the markers and selecting for therapy in a subject with a genotype that correlates with race wherein the MI gene, comprises nucleic acid that encodes 5-1ipoxygenase activating protein (ALOX5AP or FLAP) referred to as FLAP (see spec. of 11270804, page 7, lines 27-30).
Thus, the process is a set of precursor steps to the process of treating the MI and therefore are part of the obvious variation of the copending application claims compared to the current application claims.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Claims 206-209, 211-214, 216-217 and 225-228 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1-10 and 12-27** of U.S. Patent Application No. **11096191**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

The claims of the instant application and that of the co-pending refer to a method of treating myocardial infarction in human comprising administering a MI agent that inhibits leukotriene synthesis in vivo.

Both applications recite using the same compound formula. See current application claims 206-209, 211-214, 216-217 and 225-228 and copending application claims 1-10 and 12-27. The instant application is directed to methods of treatment (prophylactic and/or therapeutic) for certain diseases and conditions (e.g., MI, associated with FLAP or with other members of the leukotriene pathway (e.g., biosynthetic enzymes or proteins such as FLAP). Note that FLAP genotyping is elected.

The compositions recited in the co-pending claims are anticipatory of the claims in the instant application.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Claims 206-209, 211-214, 216-217 and 225-228 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1, 4-5, 7-9, 11-12, 23-25, 37, 40 and 43-45** of U.S. Patent Application No. **10587412**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

The claims of the instant application is to a treatment of myocardial infarction wherein the compound BAY-X-1005 is used in the treatment of the instant claim sets of claims refer to a method of treating/prophylaxis therapy for myocardial infarction in human comprising administering a MI agent that inhibits leukotriene synthesis in vivo.

Both set of application claims recite using the same compositions and/or derivatives thereof. See current application claims 206-209, 211-214, 216-217 and 225-228 and copending application claims 1, 4-5, 7-9, 11-12, 23-29, 37, 40 and 43-45. The compositions recited in the copending application are anticipatory of the claims in the instant application.

Because they would have been used in producing the markers and selecting for therapy in a subject with a particular SEQ ID NO:1 because the claims of the instant application are identifying or selecting a human subject with a FLAP genotype (see page 7, lines 11-15 of 10/587,412) as in claims 23-29. Thus, the process is a set of precursor steps to the process of treating the MI and therefore are part of the obvious variation of the copending application claims compared to the current application claims.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Claims 206-209, 211-214, 216-217 and 225-228 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 206-210, 212-222, and 245-246 of Patent Application No. 10830477. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

The claims of the co-pending application recite a method of prophylaxis or treatment for myocardial infarction by selecting the individual suffering from such and administering a leukotriene inhibitor using the compound BAY-X-1005. Similarly the claims of the instant application are to a treatment for MI in a patient administering a leukotriene inhibitor. See current application 206-209, 211-214, 216-217 and 225-228 and copending application claims 206-210, 212-222, and 245-246. The compositions recited in the copending claims anticipates the instant claims.

Thus the claims are obvious variant of the instant application. They both administer the same compound for the treatment of a cardiovascular condition, by a process of selecting the patient using a marker.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
2/25/08

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614